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SCIENCE

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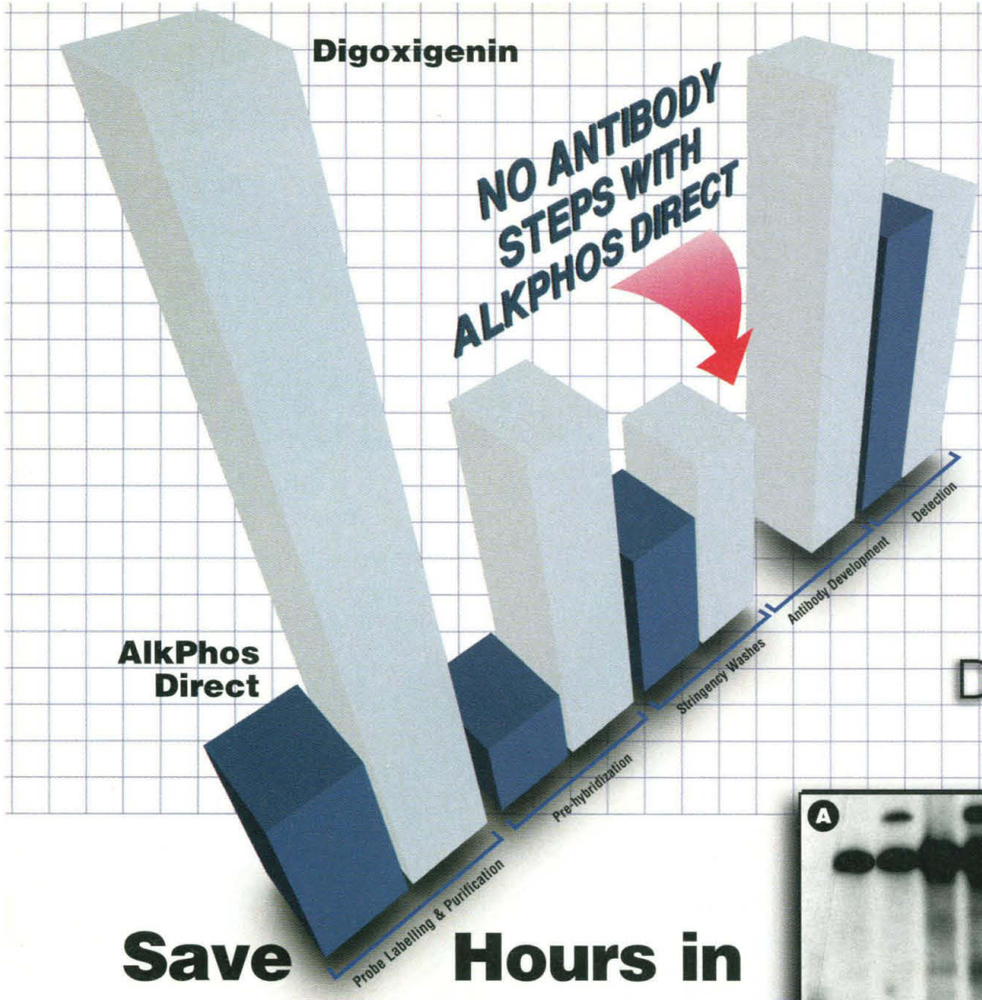

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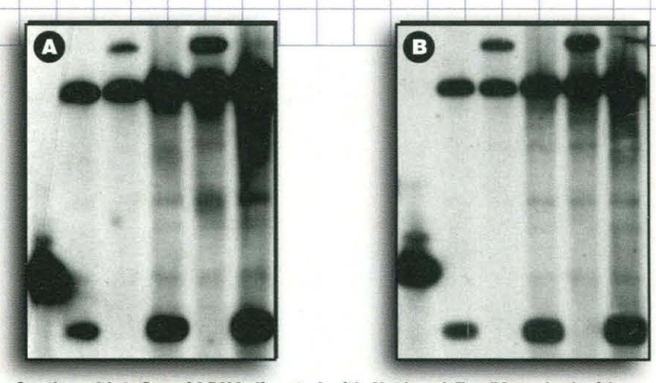

Southern blot, Cosmid DNA digested with *Not*1 and *Eco* RI, probed with a 1.1kb probe labelled with AlkPhos Direct (A) and digoxigenin (B) *(courtesy of Janet Bartels, Yale University).*

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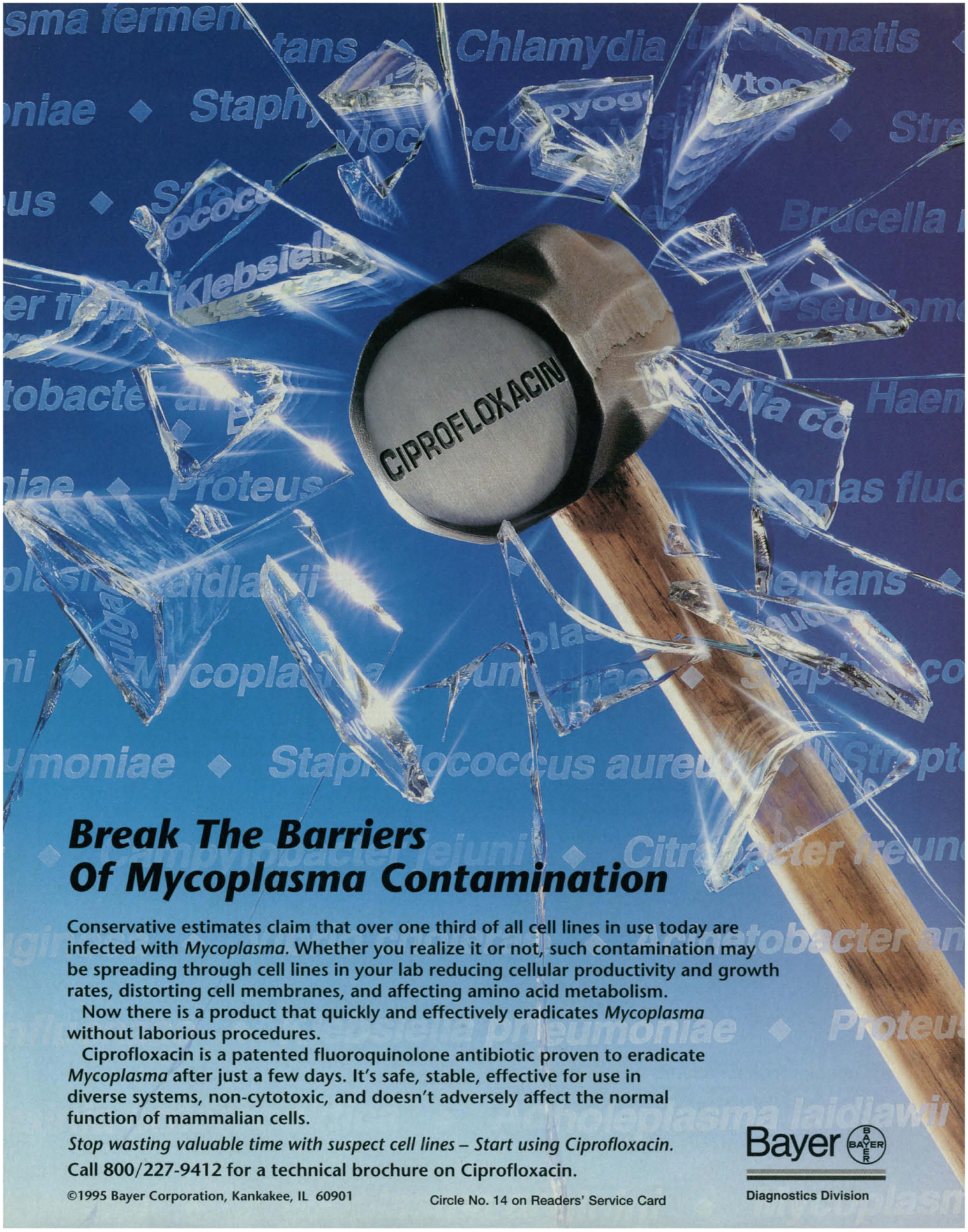

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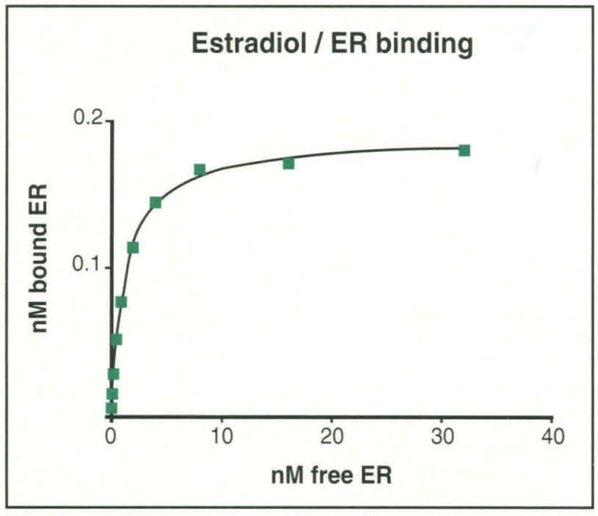

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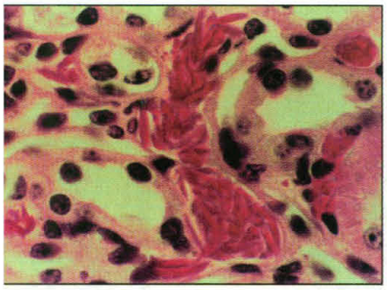
Son of Adam



803, 873 & 876
Mouse model for sickle cell disease

NEWS & COMMENT

RESEARCH NEWS

PERSPECTIVES

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DEPARTMENTS

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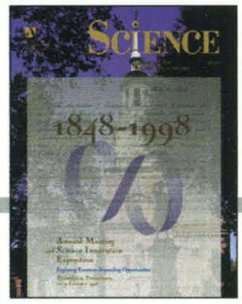
COVER

The invitation to the first meeting of what was then planned to be the American Association for the Promotion of Science. Independence Hall is pictured in the background. AAAS will open its 150th Anniversary year celebration with the Annual Meeting in Philadelphia, where the association was founded on 20 September 1848 at the Academy of Natural Sciences. See page 885 for the many special activities and speakers that will be a part of the 1998 opening. [Photo of Independence Hall: Photodisc, Incorporated. Collage: C. Faber Smith]



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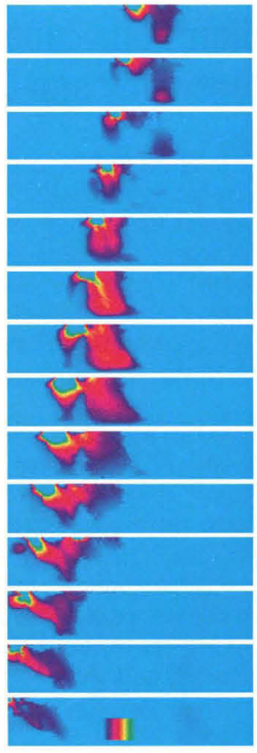

834

Yikes! Here comes the rupture

◩ Indicates accompanying feature

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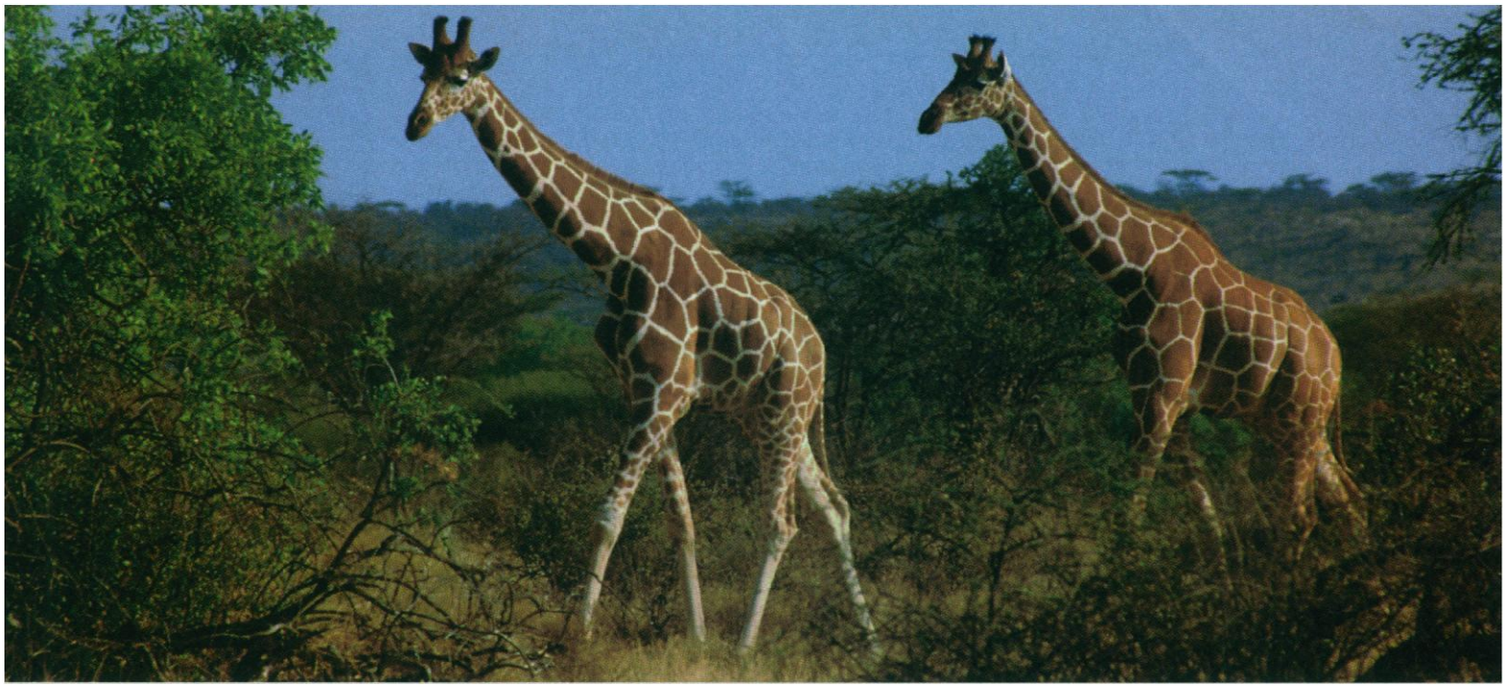

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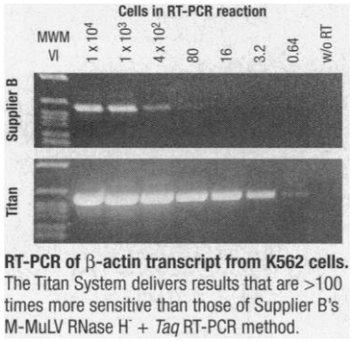

RT-PCR of β-actin transcript from K562 cells. The Titan System delivers results that are >100 times more sensitive than those of Supplier B's M-MuLV RNase H⁻ + *Taq* RT-PCR method.

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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

Mesoporous metal films

Mesoporous materials that contain nanometer-sized pores have received considerable attention recently. Most of these materials that have been made are ceramic oxides. Attard *et al.* (p. 838) now report the synthesis of mesoporous platinum films by electrodeposition of the metal from liquid-crystalline plating mixtures. Such materials could be used in applications that include catalysis, batteries, fuel cells, and sensors.

Suddenly warmer

The end of the Younger Dryas marked the abrupt (about 40-year) transition to warm climates in the Holocene; this transition has been studied closely as it provides information on the sensitivity of Earth's climate. Taylor *et al.* (p. 825) analyzed the GISP2 Greenland ice core, which provides a year-by-year account of the climate changes, and shows that this transition occurred in a series of steps each lasting less than 5 years. Some data imply that climate changes in the Arctic slightly follow changes at lower latitudes.

Re-creating an earthquake

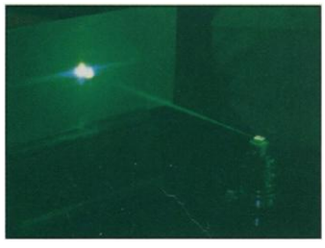
The 1992 Landers earthquake in the Mojave Desert is one of the best-characterized recent events; surface deformation could be readily measured in the desert, and seismicity was monitored before and after this magnitude 7.3 earthquake. Olsen *et al.* (p. 834) used the slip and stress distribution derived from inverting the seismic data to re-create the initial stress distribution in the area before the earthquake and then forward-modeled the rupture in three dimensions. Their rupture model fits the general pattern of ground motions from seismic recordings but also shows a complex process that includes an increasing rupture velocity as the rupture approaches the surface, which was not predicted by simpler kinematic inversions.

Mouse models for sickle cell anemia

Animal models for human diseases have been valuable for understanding the disease and designing effective therapies. Two separate groups, Pászty *et al.* (p. 876) and Ryan *et al.* (p. 873) have developed a strategy that resulted in a mouse model for sickle cell anemia (see the news story by Barinaga, p. 803). They first created mice that carried human sickle hemoglobin and then bred them with mice in which the mouse forms of α and β globin had been deleted. Progeny were identified that expressed only human hemoglobin and showed sickling of red blood cells, anemia, and organ pathologies that are characteristic of the human disease.

Quasi-periodicity in nonlinear optics

Structures that repeat not on the basis of rational numbers, such as crystals, but that repeat on the basis of irrational ratios, are quasi-periodic. Zhu *et al.* (p. 843) show that the formation of layers of a nonlinear optical material, lithium tantalate, with a quasi-periodic (Fibonacci) sequence



is useful in generating third-harmonics of laser light. The availability of more wave vectors in such a lattice allows coupling of two processes, frequency doubling and frequency adding, so that the normally weak third harmonics can be generated efficiently.

Copper chaperone in the cell

Certain enzymes in mammalian cells require metals such as copper as cofactors. However, free copper can be toxic to the cell and propagate auto-oxidation of lipids, proteins, or nucleic acids. Pufahl *et al.* (p. 853; see the Perspective by Valentine and Gralla, p. 817) describe the function of a copper chaperone protein called Atx1, which receives copper from an uptake protein in the membrane and then binds it in an unusual three-coordinate state as Cu(I). The Atx1 protein then carries the copper to its destination where Atx1 interacts with the vesicular protein Ccc2. The Cu(I) ion is passed to Ccc2 and ultimately to the multicopper oxidase Fet3, the essential enzyme in the high-affinity iron uptake system. This system allows the cell to supply copper to key enzymes without the release of copper ions directly into the cytoplasm.

Aerosols and smog production

Photochemical smog, characterized by high ground-level ozone and nitrogen oxide levels, depends partly on the intensity of solar ultraviolet radiation. Atmospheric aerosols scatter or absorb ultraviolet light, but a quantitative analysis of this effect on smog formation has been lacking. Numerical modeling by Dickerson *et al.* (p. 827) of observations of aerosols, radiation, and photochemistry indicate that smog production is accelerated by ultraviolet-scattering aerosols and inhibited by ultraviolet-absorbing aerosols.

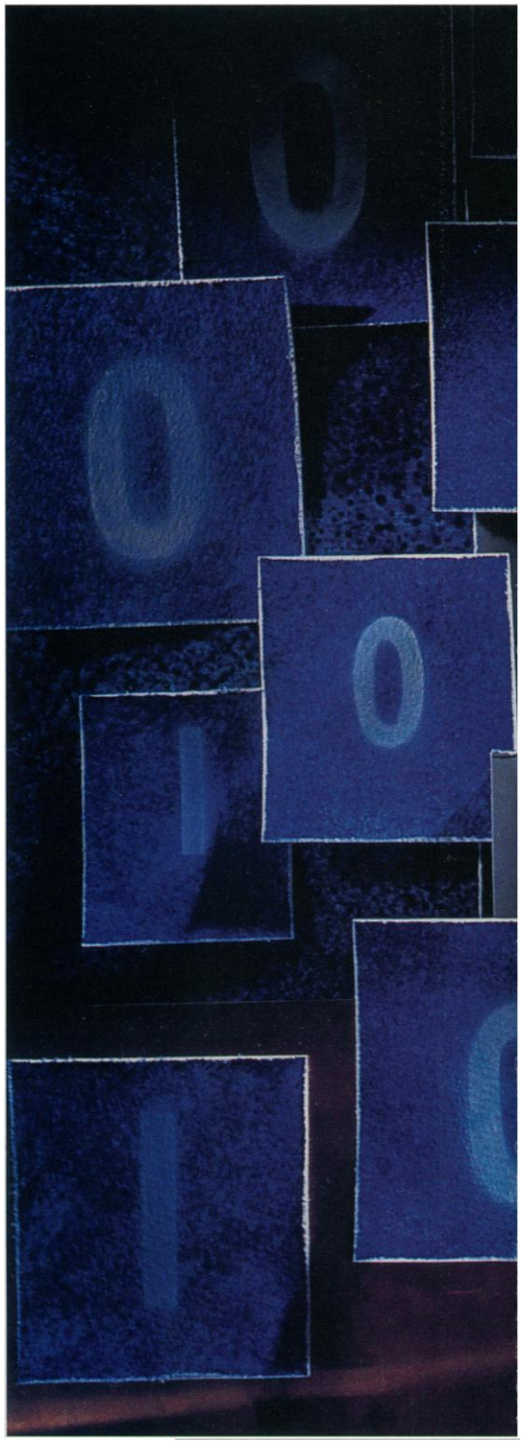
Responding indirectly

Previous assessments of global terrestrial responses to climate change have focused on direct responses to change in carbon dioxide or temperature. These near-instantaneous responses include, for example, the effects of increased temperature on photosynthesis and respiration. However, field ecologists have repeatedly suggested that indirect responses, such as feedbacks through soil water storage or nutrient cycling, may be more important. Braswell *et al.* (p. 870; see the news story by Williams, p. 802) offer a global assessment of direct versus indirect effects, and demonstrate the importance of indirect effects. The results also provide evidence at the global scale for major differences between biomes in both the direction and strength of these indirect effects: Large-scale modification of global ecosystems could alter the response of the biosphere to climate change.

Cytokines and NF-κB

The transcription factor NF-κB is critical for regulation of gene transcription in cells of the immune system. Two reports discuss identification of a new component of a regulatory pathway that controls the activity of NF-κB in response to cytokines like tumor necrosis factor–α or interleukin-1 (see the Perspective by Maniatis, p. 818). NF-κB is held in an inactive state by the protein IκB, and interaction of the two proteins is controlled by phosphorylation of IκB. A protein kinase (IκB kinase or IKK-1) that participates in this regulation has been recently described. Mercurio *et al.* (p. 860) and Woronicz *et al.* (p. 866) now report isolation and characterization of a second member of the IKK family (IKK-2). The two IKKs interact with each other and with another protein kinase, NIK, in a large protein complex.

WHAT IF YOU COULD CREATE A DRUG THAT WAS INACTIVE UNTIL IT WAS "SWITCHED ON" AT THE TARGET SITE?



Doctors want drugs powerful enough to destroy a disease. But they also seek to leave healthy parts of the body unharmed.

Much of medicine is an unending search for a delicate balance between these contrary goals.

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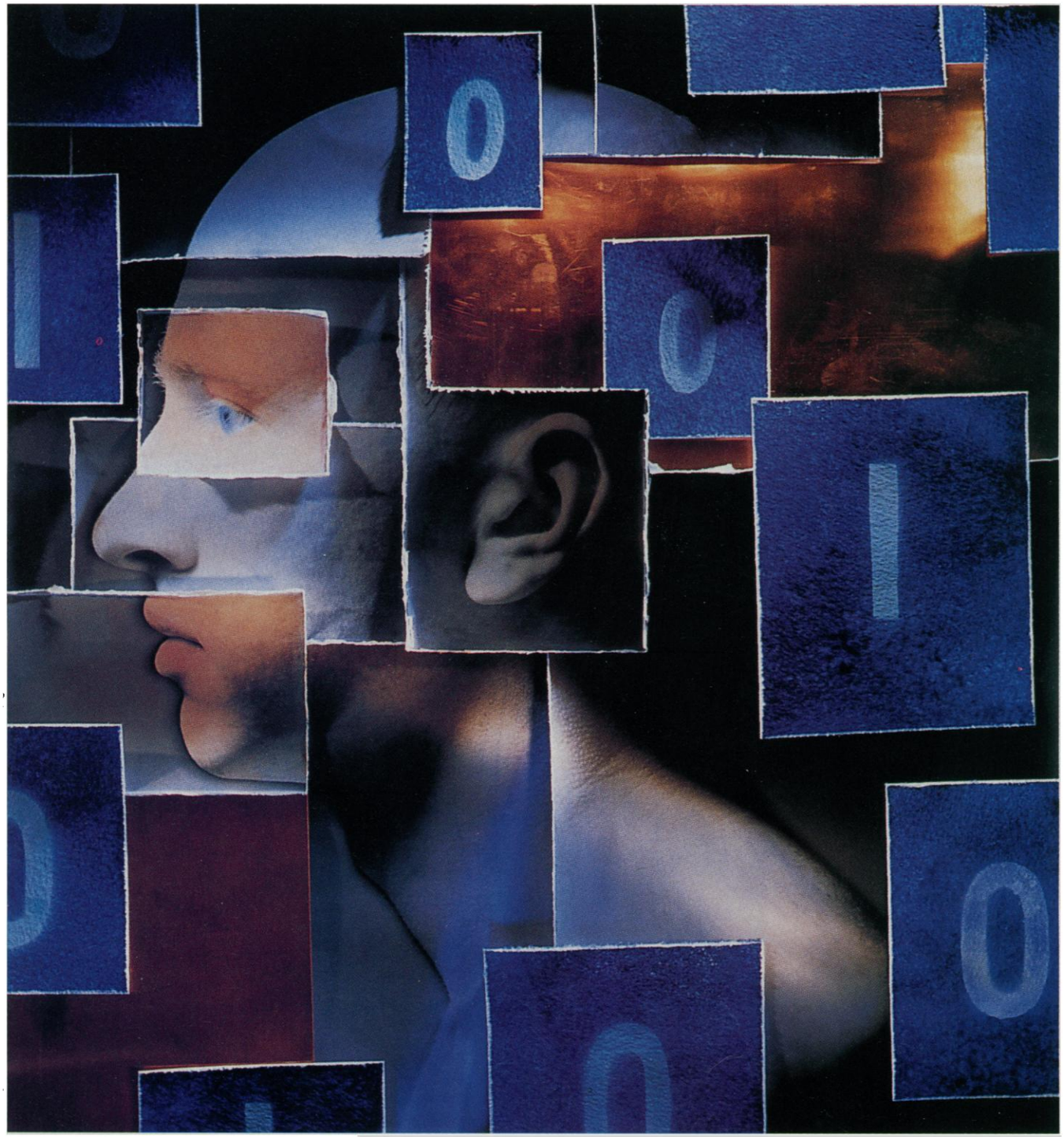

Targeted cells are destroyed by an interaction between the drug and the light, with minimal known side effects. PhotoPoint, now in clinical trials, is being developed as an outpatient procedure.

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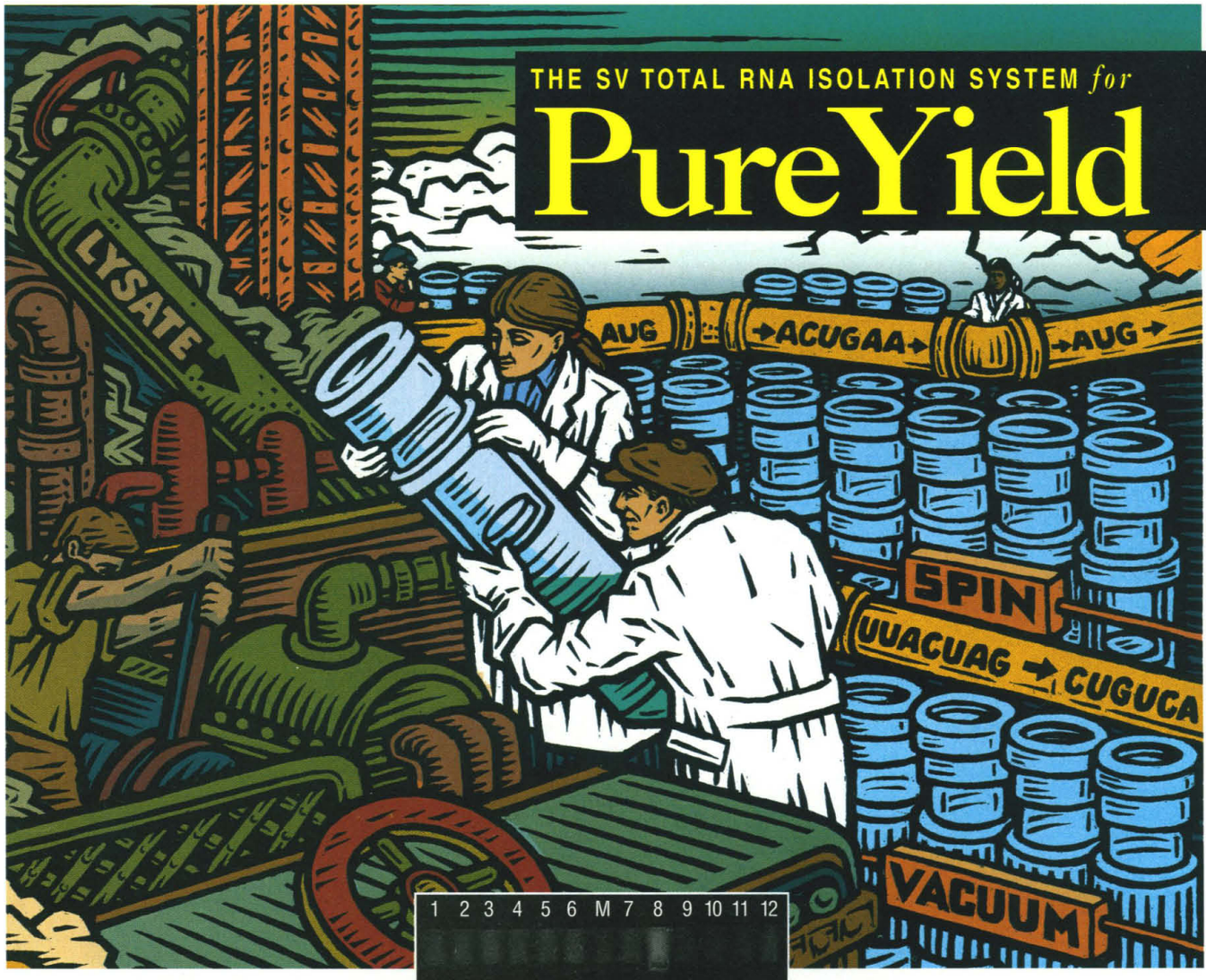

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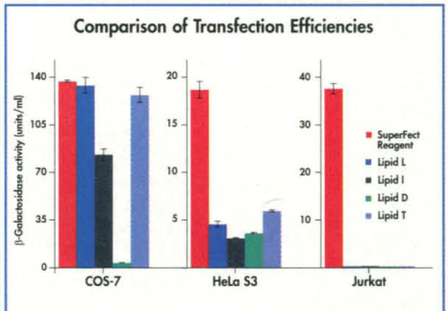

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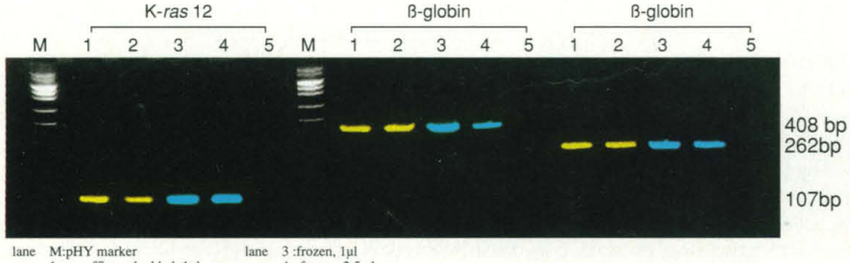
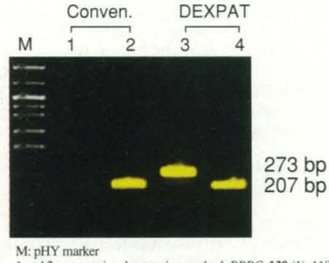
Comparison of Section Preparations
for K-*ras* 12 (107 bp) and ß-globin (408 bp and 262 bp) Amplification from Human Tonsil: 1 µl or 2.5 µl extracts used for 25 µl PCR



lane M:pHY marker
1 : paraffin-embedded, 1µl
2 : paraffin-embedded, 2.5 µl
3 :frozen, 1µl
4 : frozen, 2.5 µl
5 : negative control

Comparison of Extraction Methods
for p53 *exon* 5 (273 bp) and *exon* 6 (207 bp) Amplification from Paraffin-embedded Tissues of Colon Cancer After a 10-year Preservation



lane M: pHY marker
1 and 2 : conventional extraction method: *BBRC* **130** (1), 118-126 (1985)
3 and 4: newly developed TaKaRa DEXPAT™ method

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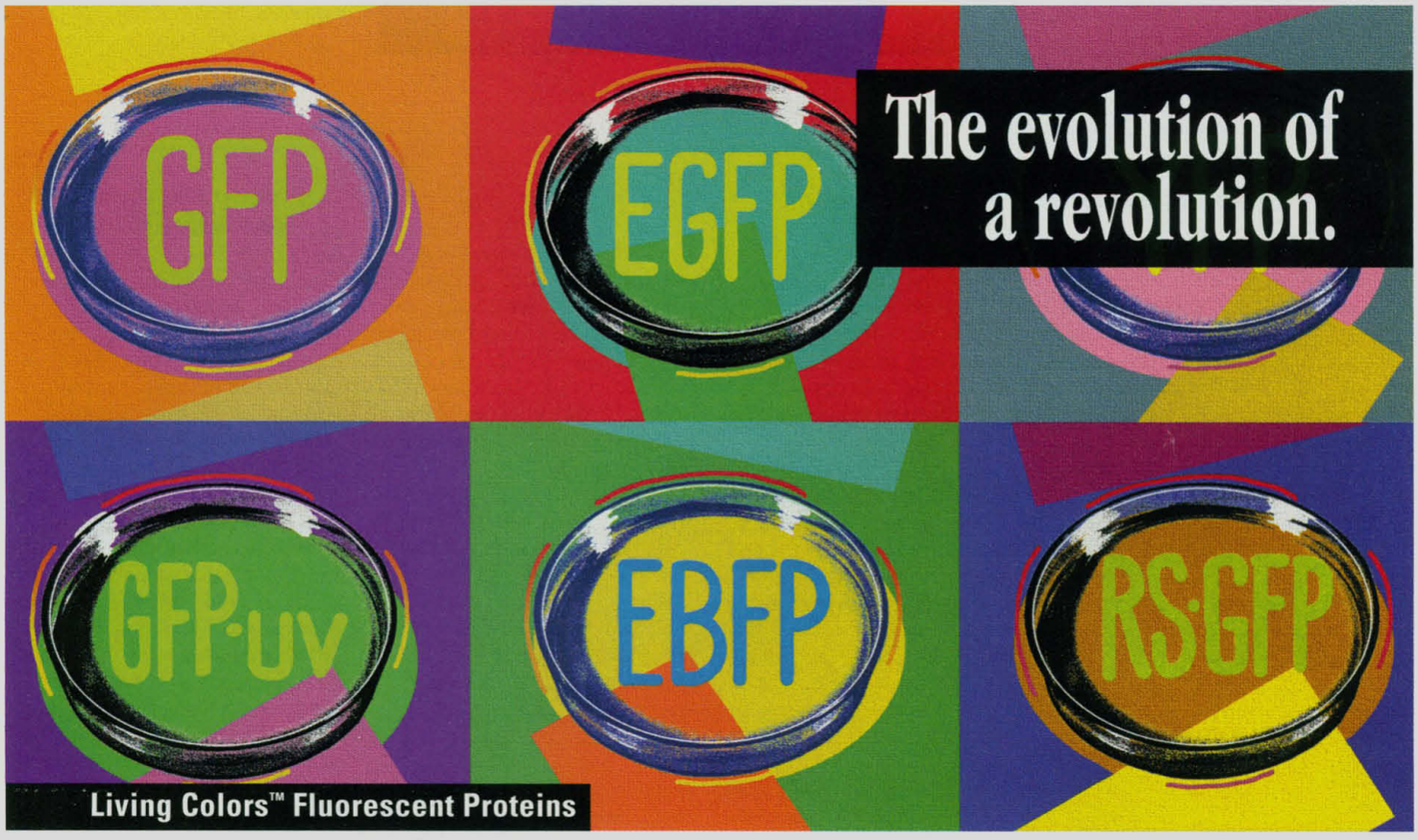
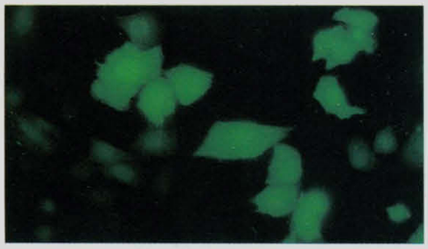


Expression of EBFP in fixed 293 EBNA cells.



Expression of EGFP in fixed CHO-K1 cells.

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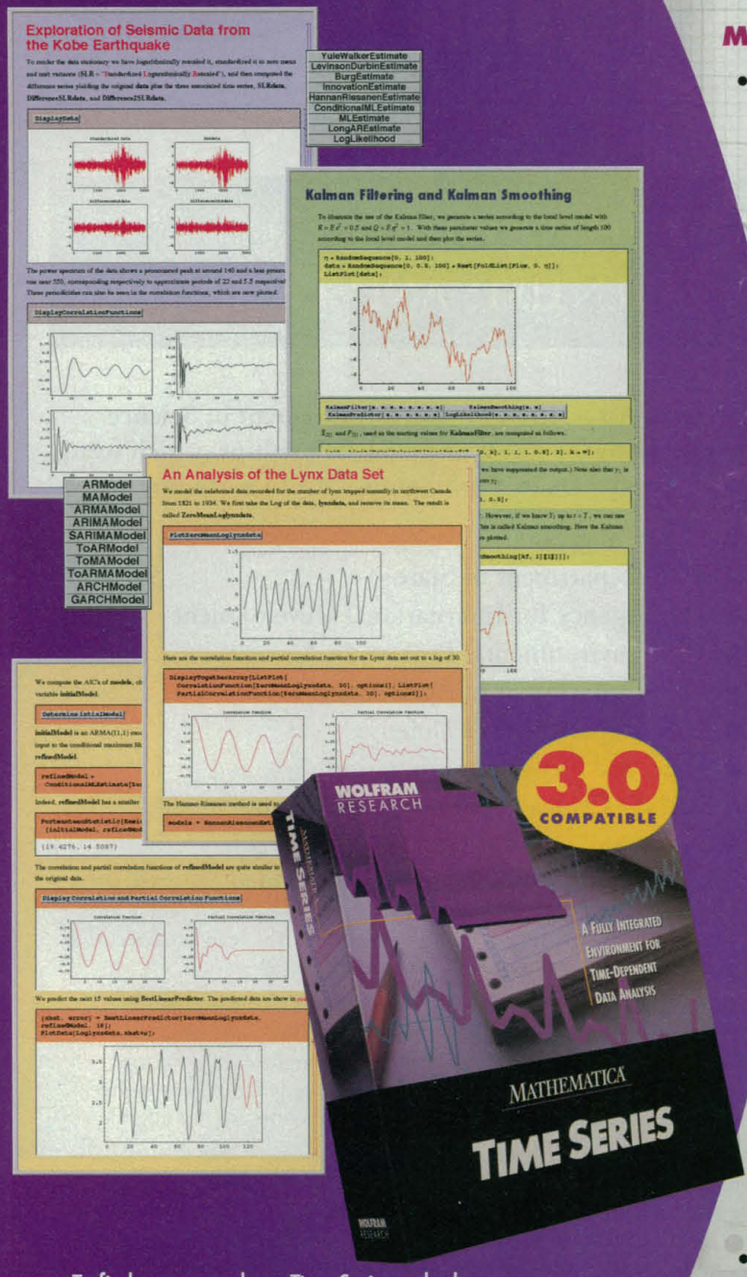

Models

- Stationary time series models: AR, MA, ARMA
- Nonstationary time series models: ARIMA, SARIMA
- Univariate and multivariate time series models
- Structural models: State-space form and the Kalman filter
- ARCH and GARCH models
- Covariance, correlation, and partial correlation functions

Model Identification

- Estimation of sample covariance, correlation, and partial correlation functions
- Akaike's Information Criterion (AIC)
- Bayesian Information Criterion (BIC)

Parameter Estimation

- Yule-Walker, Levinson-Durbin, Burg's, innovations, and long autoregression algorithms
- Hannan-Rissanen procedure
- Maximum likelihood method

Diagnostic Checking

- Residuals
- Portmanteau test
- Information matrix

Forecasting

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Spectral Analysis

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- Spectrum estimation
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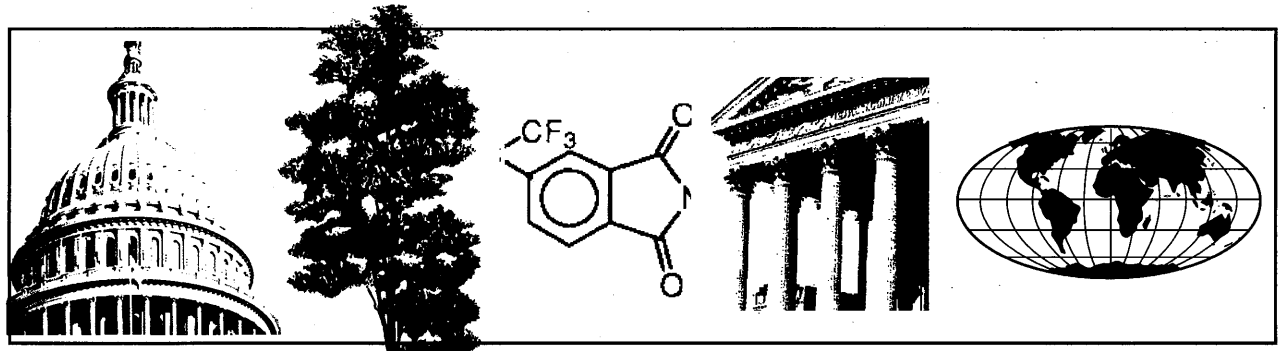

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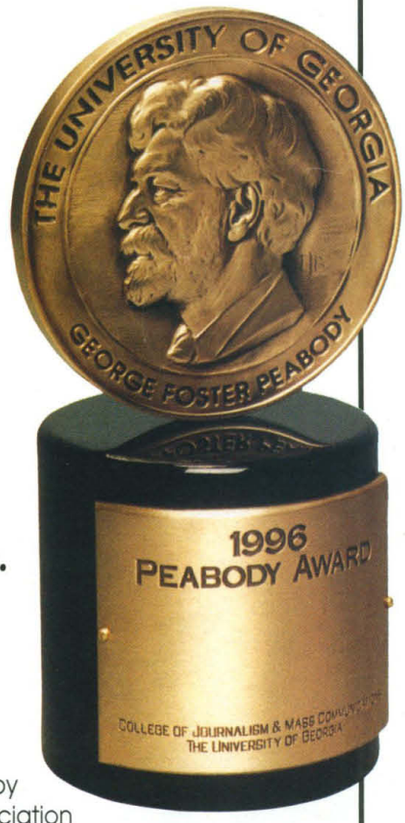

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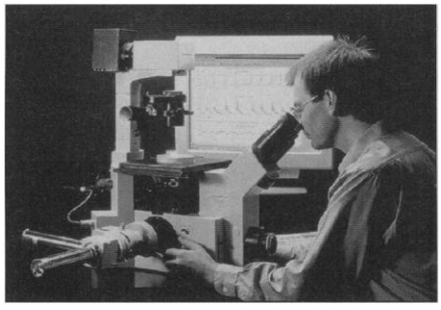

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